

REMARKS**I. Status of the Application**

Claims 1-8, 10-56 are presently pending in the application. Claims 16-36, which are directed to a non-elected invention, have been cancelled without prejudice to the filing of any appropriate continuation applications. Applicants gratefully acknowledge that the indefiniteness rejection of claim 10 has been withdrawn, and the written description and enablement rejections of claims 40-56 have been withdrawn. Claims 1-8 and 39-49 stand rejected under 35 U.S.C. §112, first paragraph, as lacking enablement. Claims 1-8 and 39-49 stand rejected under 35 U.S.C. §112, second paragraph, as being incomplete for omitting essential steps. Claims 1-8 and 39-49 stand rejected under 35 U.S.C. §102(e) as being anticipated by Holmes, U.S. Patent No. 5,679,773.

Applicants have amended the claims in their response dated June 20, 2005 and in the present amendment to more clearly define and distinctly characterize Applicants' novel invention. In the present amendment, applicants have deleted reference to cleavable linkers in claims 1 and 40 to be more consistent with allowed claims 10 and 50. In the amendment of June 20, 2005, claims 1 and 40 were amended to recite "predicting a quantity of diverse [biological] polymers formed and comparing a measurement of quantity of diverse cleaved [biological] polymers with the predicted quantity of diverse [biological] polymers formed as an indicator of the efficiency of the synthesis procedure, thereby determining the efficiency of the synthesis procedure." As indicated in the June 20, 2005 response, support can be found in the specification at least at page 18, lines 11-16 where Applicants teach assaying the efficiency of polymer synthesis cleaved from an array by comparing the cleaved polymers with predicted size and charge values and at page 39 lines 9-18 where a method of determining the quantity of polymers cleaved from an array is disclosed. Applicants respectfully submit that based on the

specification as a whole, one of skill in the art would be in possession of the invention where the quantity of the polymer is predicted and compared with the measured quantity.

The amendments presented herein add no new matter. Applicants respectfully request entry and consideration of the foregoing amendments and consideration of the following remarks, which are intended to place this case in condition for allowance.

II. Claims 1-8 and 39-49 Are Enabled

At page 3, section 11 of the instant Office Action, claims 1-8 and 39-49 stand rejected under 35 U.S.C. §112, first paragraph, as not being enabled. The Examiner is of the opinion that the instant claimed method is drawn to monitoring the polymer array synthesis, but that the claims do not recite how the presence of unbound biological polymers indicate the efficiency of the synthesizing step. The Examiner requests that Applicants include method steps used to measure the efficiency of the synthesis. Applicants respectfully traverse this rejection.

Without acquiescing to the rejection, Applicants respectfully submit that amended claims 1 and 40 recite a method of monitoring polymer array synthesis comprising synthesizing a preselected array of diverse [biological] polymers on a solid substrate, cleaving the diverse [biological] polymers from the solid substrate, *predicting* a quantity of diverse biological polymers formed and *comparing* a measurement of quantity of diverse cleaved biological polymers from the array with the predicted quantity of diverse biological polymers formed as an indicator of the efficiency of the synthesis procedure, thereby determining the efficiency of the synthesis procedure. Thus, the efficiency of the reaction is determined by a step in which the quantity of diverse cleaved polymers formed is compared with predicted quantity.

Applicants teach that "a preselected array of polymers" is a spatially defined pattern of polymers on a solid support which is designed *before* being constructed wherein the arrangement

of polymers on a solid substrate during synthesis is *deliberate* (page 15, lines 25-29). Given that the practitioner would know the density of polymers formed on the array as well as the concentration of polymer components used to synthesize polymers on the array, one of skill in the art could easily estimate the quantity of polymers that could be formed on the array based on this information. Once the quantity of diverse polymers formed is predicted, this prediction can be compared with the quantity of cleaved polymers that were synthesized on the array in order to determine efficiency of synthesis. Applicants teach that measurements such as the length distribution of synthesized species, the presence, nature and extent of truncated species, and electrostatic charge of synthesized species, are all useful physical parameters for comparison with predicted values (page 18, lines 11-16). Applicants further teach measuring the quantity of polymers formed using such techniques as HPLC at page 39 lines 9-18.

Therefore, Applicants' specification, coupled with the level of skill and knowledge in the art of polymer arrays enables one skilled in the art to make and/or use the claimed invention. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the rejection of claims 1-8 and 39-49 under 35 U.S.C. § 112, first paragraph.

III. Claims 1-8 and 39-49 Clearly Recite Method Steps

At page 3, section 12 of the instant Office Action, claims 1-8 and 39-49 stand rejected under 35 U.S.C. §112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. The Examiner is of the opinion that the step of measuring to determine the efficiency of the synthesis step is omitted. The Examiner states that it is not clear how measuring the unbound polymer is an indication of the efficiency of the synthesis step and that the efficiency of the synthesis step depends on several variables, such as reaction conditions, that is, reagents used, cleavable linkers used, the solid support surface, or the

different cleavable linkers used. The Examiner requests that Applicants include a step indicating how the efficiency of the synthesis step is measured. The Examiner is further of the opinion that there is no correlation between the method steps 'a method of monitoring polymer array synthesis on a solid substrate' and 'measuring the presence of diverse unbound polymer as indicator of efficiency of the synthesizing step'. The Examiner requests that Applicants amend the claim to clearly recite the method steps. Applicants respectfully traverse this rejection.

However, without acquiescing to the rejection, Applicants respectfully submit that claims 1 and 40 have been amended to delete the reference to cleavable linkers to make them more consistent with allowed claims 10 and 50. Claims 1 and 40 have also been amended to recite the step of "predicting a quantity of diverse [biological] polymers formed and comparing a measurement of quantity of diverse cleaved [biological] polymers from the array with the predicted quantity of diverse [biological] polymers formed as an indicator of the efficiency of the synthesis procedure, thereby determining the efficiency of the synthesis procedure" solely to expedite prosecution.

Thus, the pending claims clearly recite method steps. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the rejection of claims 1-8 and 39-49 under 35 U.S.C. § 112, second paragraph.

IV. Rejection of Claims 1-8 and 39-49 Over Holmes

At page 4, section 14 of the instant Office Action, claims 1-8 and 39-49 stand rejected under 35 U.S.C. §102(e) as being anticipated by Holmes, U.S. Patent No. 5,679,773. The Examiner is of the opinion that Holmes teaches that following the synthesis of the attached labeled polymer, the fidelity of synthesis can be determined by cleaving labeled polymer from the support, subjecting the labeled polymers to high performance liquid chromatography and

comparing the resultant chromatogram with a chromatogram from a standard which is synthesized by an alternate method. The Examiner concludes that Holmes clearly anticipates the claimed invention. Applicants respectfully traverse this rejection.

Holmes neither teaches nor suggests the claimed invention. Holmes fails to disclose measuring the quantity of diverse cleaved [biological] polymers as an indicator of the efficiency of the synthesizing step, as recited in claims 1 and 40. Nor does Holmes teach the claimed step of *predicting a quantity of diverse biological polymers formed and comparing a measurement of quantity of diverse cleaved [biological] polymers* from the array with the predicted quantity of diverse biological polymers formed *as an indicator of the efficiency* of the synthesis procedure, thereby determining the efficiency of the synthesis procedure, as recited in claims 1 and 40.

Holmes merely teaches ascertaining synthesis *fidelity* by comparison with known standards (column 19, lines 34-48). Holmes uses HPLC in their determination whether the desired product was faithfully produced (column 30, lines 16-19). Holmes teaches that their samples are subjected to HPLC and that the resulting chromatogram is compared with a chromatogram from a standard which was synthesized by alternative methods (column 22, lines 16-23). Nowhere does Holmes teach or suggest ascertaining the *efficiency* of their synthetic methods by predicting a quantity of diverse [biological] polymers formed and comparing a measurement of the quantity of diverse cleaved [biological] polymers from the array with the predicted quantity of diverse [biological] polymers formed, as claimed by Applicants.

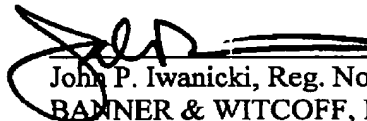
Accordingly, Holmes fails to teach or suggest each and every element of Applicants' claimed invention. Therefore, Applicants request that the rejection of claims 1-8 and 39-49 under 35 U.S.C. § 102(e) as being anticipated by Holmes be reconsidered and withdrawn.

V. Conclusion

Having addressed all outstanding issues, Applicants respectfully request entry and consideration of the foregoing amendments and reconsideration and allowance of the case. To the extent the Examiner believes that it would facilitate allowance of the case, the Examiner is requested to telephone the undersigned at the number below.

Respectfully submitted,

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